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ORIGINAL ARTICLE

Alkyl-malonate-substituted thiacalix[4]arenes as ligands for bottom-up design of paramagnetic Gd(III)-containing colloids with low cytotoxicity

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Abstract The present work introduces thiacalix[4]arene adopting 1,3-alternate conformation with alkyl-malonate terminal substituents as ligands for Gd(III) ions. pH-dependent complex formation of Gd(III) ions via alkyl-malonate substituents in aqueous DMSO solutions results in a precipitation. The precipitated complexes were converted into hydrophilic colloids of "plum-pudding" morphology, where the Gd(III) complexes form hard small (1.5–4 nm) cores included into larger (about 180 nm) soft PSS shells. The precipitate-to-colloid transformation is facilitated by polystyrolsulfonate (PSS) for Gd(III) complexes with thiacalix[4]arene bearing propyl-malonate groups, while the presence of PSS triggers a dissolution of the precipitated complexes for thiacalix[4]arenes with pentyl-malonate substituents. To a lesser extent the similar tendency disturbs the formation of PSS-stabilized colloids on the basis of butyl-malonate substituted thiacalix[4]arene. The PSS-stabilized colloids exhibit high longitudinal and transverse relaxivities (r_1 = 23.8 and r_2 = 29.4 mM^{-1} s^{-1} at 0.47 T, respectively), while the recoating of the PSS-stabilized colloids with polyethyleneimine is accompanied by the dissolution of the hard cores. High relaxivity along with low cytotoxicity of PSS-stabilized colloids indicates their applicability as contrast agents in MRI.

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1. Introduction

Gd(III) complexes have attracted significant attention in recent decades due to their use in MR imaging (Burtea et al., 2008; Lauffer, 1988; Platzek et al., 1997). Many commercial MRI contrast agents are based on Gd(III) complexes (Burtea et al., 2008; Platzek et al.,

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